

REMARKS

The claims have been amended to limit them to mammalian laboratory animals, a limitation which is clearly supported by the specification. See, for example, page 4, at lines 22-24; page 5, lines 5-18; page 5, lines 29, *et seq.*, and throughout the specification. Thus, no new matter is added.

Applicants respectfully request that the Examiner exercise her discretion and enter this amendment though made after final. The amendment clearly places the claims in a position for allowance as the limitation overcomes the outstanding rejection. Applicants further have not had an opportunity to address the Link reference cited in the outstanding rejections previously, so applicants believe, in fairness, they should be permitted this opportunity. Entry of the amendment is therefore respectfully requested.

Applicants very much appreciate the withdrawal of the rejections that had been made previously.

The rejection of claim 37 under 35 U.S.C. § 103 over newly cited Link, *et al.* (*Cell Stress and Chaperones* (1999) 4:235-242

Link describes transgenic *C. elegans* that express jellyfish GFP under control of an endogenous promoter. To that extent, Link is related to the claimed subject matter. However, there are two explicit limitations in the claim that are neither disclosed nor suggested by Link.

The first, of course, is the limitation to mammalian subjects. This limitation is not arbitrary, or meaningless because the nature of mammalian subjects with regard to the techniques claimed is greatly different from that of *C. elegans*. Specifically, *C. elegans* is a transparent organism which makes observation of fluorescence in the intact subject trivial. (See the highlighted portions on page 2 of the attached description, as well as the illustration on page 1 thereof.) Thus, work

conducted in a transparent organism would certainly not suggest successful outcomes in opaque subjects such as mammals.

Second, the claims require that the animal is mobile and not restrained. The Office appreciates that Link does not explicitly state that *C. elegans* is mobile; indeed it is not – as will be shown below. However, the Office appears to believe that the *C. elegans* as disclosed in Link is inherently actually mobile when observed. This is not the case, and Link makes this clear.

Page 237 describes “Photomicroscopy and Quantitation of GFP Levels.” In the upper right-hand corner, it is noted that the animals were “mounted on 2% agarose pads and observed under a cover slip.” They could thus not be mobile while being observed. Further, the same animals were never observed more than once. The description goes on to say “to avoid repeated re-mounting of animals, a given cohort was assayed at only one timepoint.” Thus, the repetitive measurements are made on different cohorts of *C. elegans* which do not, therefore, need even to remain alive between observations.

Accordingly, applicants believe that Link explicitly discloses that the *C. elegans* has been immobilized for observation. The ability of the applicants to observe expression while the animals are completely mobile is entirely new and not suggested by Link.

In view of these two limitations that are not only not suggested, but taught away from, by Link, applicants request that this basis for rejection be withdrawn.

Claims 39 and 40 were rejected as assertedly unpatentable over Link, et al., in view of Lin, et al. (US 6,380,458).

First, this basis for rejection may be withdrawn for the same reasons as those advanced with regard to claim 37 over Link alone. Link does not supply the teaching of obtaining whole body

fluorescence from a mammalian laboratory animal nor does it suggest that the animal be completely mobile while being observed. Lin does not remedy these deficiencies which are relevant to the subject matter of claims 39 and 40 as well as to that of claim 37. The zebrafish used by Lin are also transparent, and according to column 23, at lines 27, *et seq.*, the embryos were anesthetized, and therefore could not be mobile.

Thus, for this reason alone, the combination of Link and Lin fail to suggest the invention of claims 39 and 40.

Claim 39 also requires administering a mutation-inducing agent to obtain mutants and comparing expression in the putative mutants with that in un-mutated animals. It is correct that column 11, lines 10-18 supply the mutation/comparison aspects of claim 39, but this is insufficient to overcome the inadequacy of the disclosures in combination to suggest mammalian subjects (which are not transparent) and maintaining mobility during observation.

In short, there is nothing in either Lin or Link suggesting two crucial limitations of the claims – mobility during imaging and the use of non-transparent mammalian subjects.

Conclusion

In view of the foregoing – the failure of the cited documents to teach two critical elements of the invention or to suggest them, applicants believe that claims 37 and 39-40 are in a position for allowance and passage of these claims to issue is respectfully requested.

Should minor issues remain that could be resolved over the phone, a telephone call to the undersigned would be appreciated.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any

